Patient Learning and Advertising in the Diffusion of Cox-2 Inhibitors

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Information issues on prescription drug

- Uncertain about
  - Overall drug quality: drug efficacy, side effects.
  - Drug-patient match
- FDA
  - Clinical trials before approval (short-term)
  - Clinical trials after approval (long-term)
  - Patient feedbacks
  - FDA updates are discrete and infrequent
- Drug manufacturer
  - Clinical trials / patient feedbacks
  - Advertising towards doctors and consumers
  - Information from manufacturer may be selective and biased
- How do physicians resolve the uncertainty?

Our focus

- Physicians observe:
  - FDA approval/warnings
  - Manufacturer advertising
  - News and medical journals
  - Patient experience
- Two types of learning:
  - Across-patient learning: the overall drug quality
  - Within-patient learning: drug-patient match

Our contribution

- Combine across-patient and within-patient learning in one model
  - Liter on across-patient learning:
    - Ching (2005), Coselli and Shum (2003), Narayanan et al. (2005)
  - Liter on within-patient learning:
    - Crawford and Shum (2005)
- Unique data
  - Patient satisfaction
  - Direct-to-doctor advertising
  - Direct-to-consumer advertising
  - News coverage and medical articles

IPSOS Satisfaction data

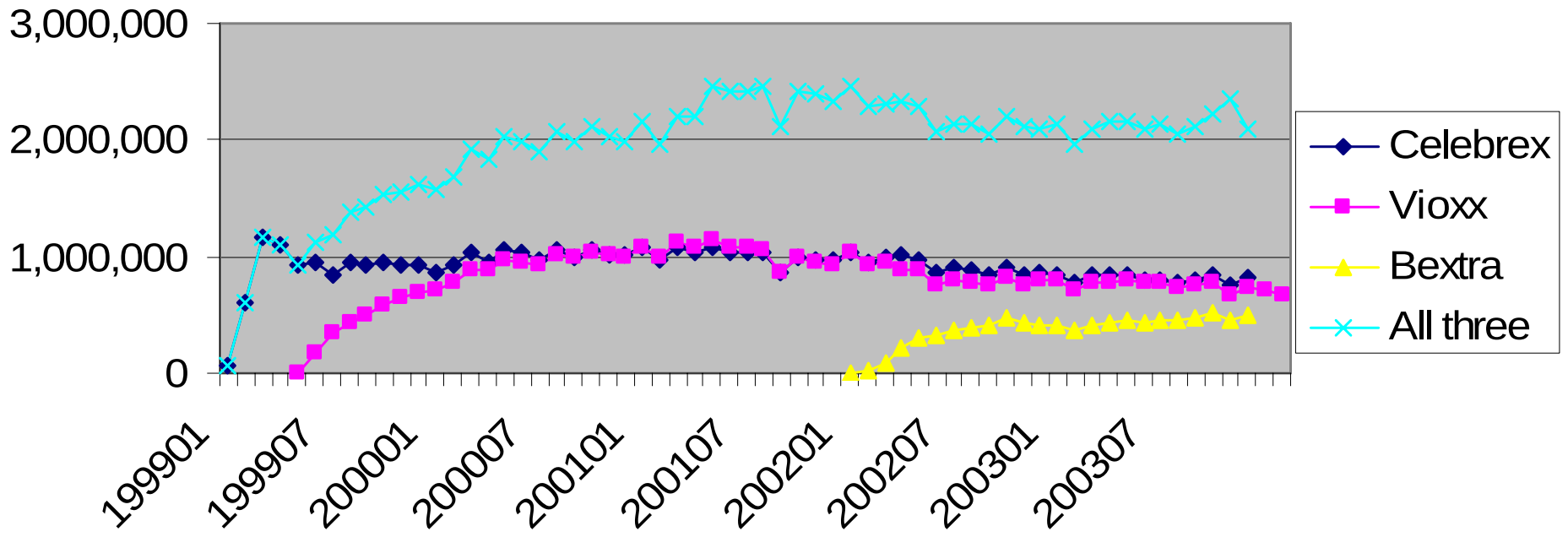
- Marketing research company, IPSOS, tracks a national representative sample of drug patients
- Reports every prescription received by the sampled patients
- Longitudinal record of patient satisfaction since January 2001. Both efficacy and side effect profiles
- Satisfaction measures, together with the advertising intensity and media coverage, allows us to associate prescriptions with various sources of information.

Cox-2 Inhibitors

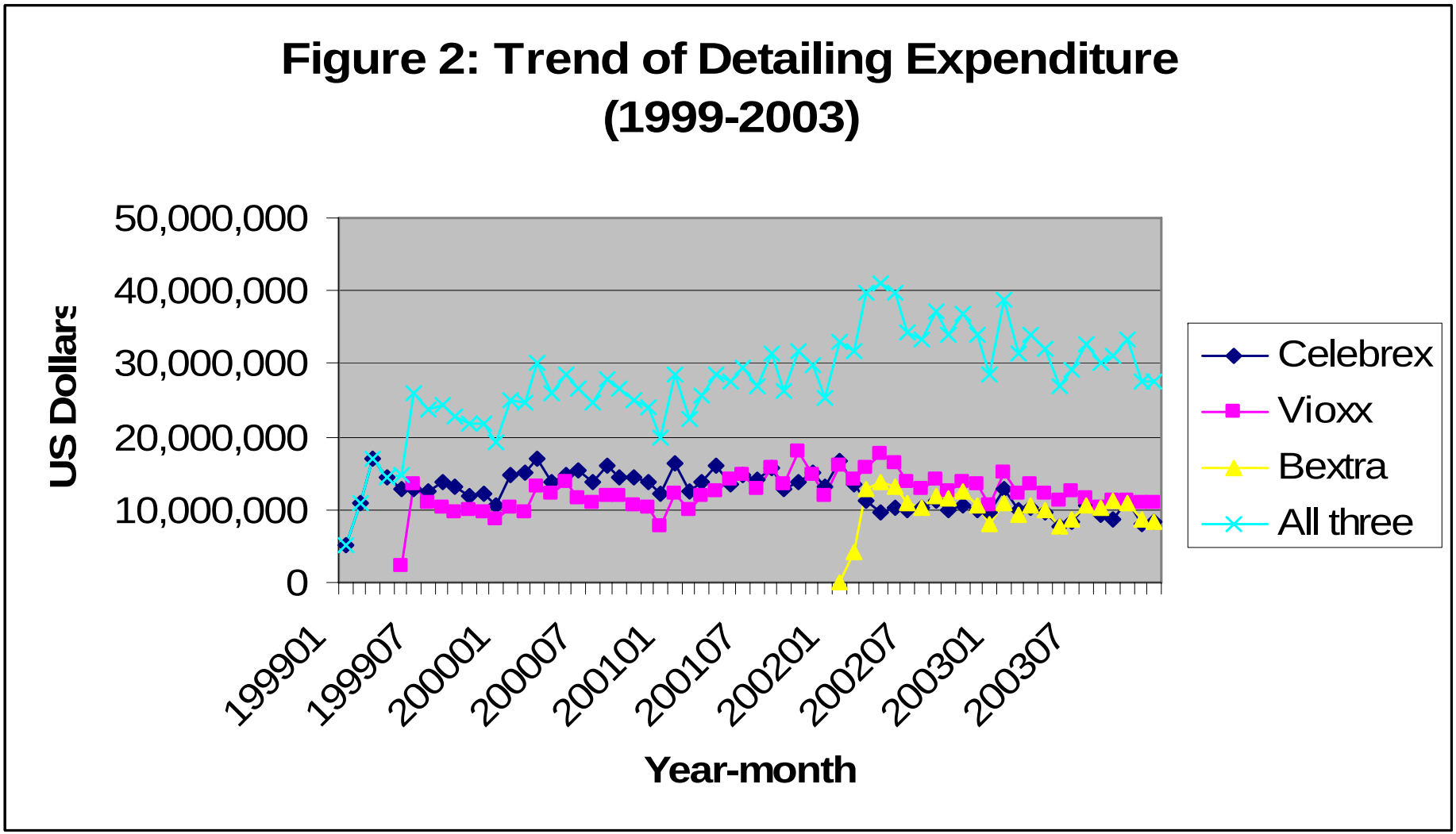
- FDA approved three Cyclooxygenase-2 (Cox-2) Inhibitors: Celebrex (Dec. 1998), Vioxx (May. 1999), and Bextra (Nov. 2001)
- Heavily advertised as safer alternatives to the existing pain killers
- By September 2004
  - More than 10 million patients
  - Annual sales reached $6 billion in 2003
  - Advertising dollars spent in 2003 were as high as $400 million
- Clinical trial associated Vioxx with severe cardiovascular (CV) risks, Merck withdrew the blockbuster drug in September 2004
- CV risks and enhanced concerns on skin irritation led to the withdrawal of Bextra in April 2005.
- As of today, Celebrex is the only Cox-2 Inhibitor remaining on the market, with warnings added in April 2005.

Data used (2001 – 2003)

Figure 1: The Number of New Cox-2 Prescriptions (1999-2003)

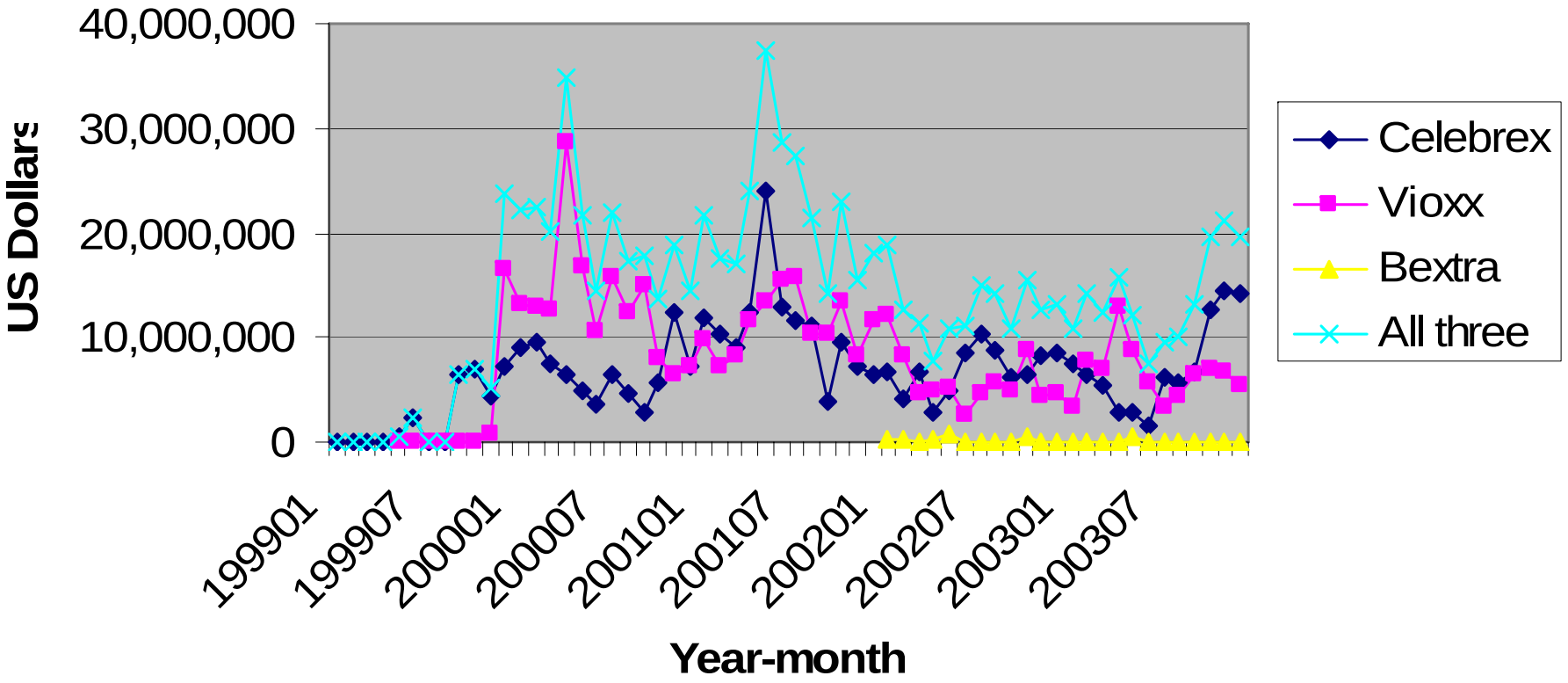


Data used (2001 – 2003)



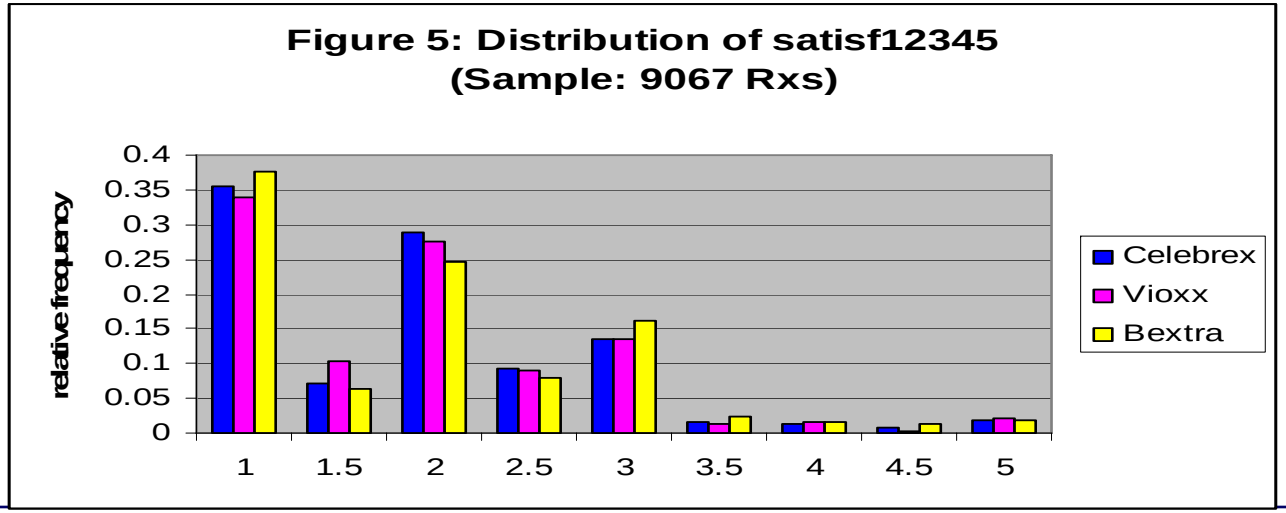
Data used (2001 – 2003)

Figure 3: Trend of Direct-to-Consumer Advertising (1999-2003)



Summary of satisfaction scores (1=extremely satisfied, 5=extremely dissatified)

	Celebrex	Vioxx	Bextra
Efficacy (satisf134)	1.929	1.924	1.988
Side effects	1.839	1.845	1.835
Easy to take	1.397	1.353	1.414
Satisf12345	1.805	1.794	1.843



Is there evidence of learning in the data?

- Average switch rate
  - Celebrex (7.92%), Vioxx (9.60%), and Bextra (10.7%)
- Regress brand switching on patient satisfaction
  - drug efficacy (coeff=0.25, t=4.03)
  - side effects (0), easy-to-take (0)
- Regress # of new patients (by drug-month) on patient satisfaction
  - Lagged satisf12345 (coeff=-19.3, t=1.7)
  - DTCA (coeff=9.4, t=3.2)
  - Detailing, JNL advertising, free samples (0)

Model assumptions

- Assume doctor is a perfect agent for the patient, because we have no data on individual doctors.
- Doctors share patient experience within a geographic area
- Focus on prescription choice within Cox-2s, as our data do not allow us to consider the potential tradeoff between Cox-2s and traditional NSAIDs.
- Doctor considers all the drug information available up to t, but no forward-looking does not consider how it would affect her future prescription choice on the same or other patients.
  - Simplifies the econometric model
  - Potential risk of mal-practice is likely to prevent doctors from experimenting

Model setup

- Patient p's CARA utility from a prescription of drug j
- True effect of drug j on patient p is $Q_{pj} = Q_j + q_{pj}$
- Doctors are uncertain about :

  Q_j =Overall quality of drug j that applies to every patient

  Q_{pj}=Match value between drug j and patient p

- Doctors have beliefs about Q_j and q_{pj} (i.i.d.)
- Each prescription generates a signal

$$R_{pjt} = \alpha_0 + \alpha_R.(Q_j + q_{pj}) + v_{pjt}$$

α_0, α_R : Scale factors

$$v_{pjt} \sim N(0, \sigma_v^2)$$

- Based on patient experiences, doctors form posteriors on Q_j and q_{pj}

Choice probabilities

$$\Pr_{pjt} = \frac{\exp(U_{pjt})}{\sum_{k=1}^{J} \exp(U_{pkt})}$$

$$U_{pjt} = \bar{Q}_{pjt} - \frac{1}{2}\gamma\sigma^2_{\tilde{Q}_{pjt}} + \beta_{xj} X_{pt} + \beta_z Z_{jt}$$

Estimation Sample

- Patients starting on or after January 1, 2001
  - 2,062 patients
  - 5,688 Rxs
- Cover 9 census regions, assume info pooling by region
- Control for age, gender
- 90% with drug insurance, drug copay reported but dirty
  - This version does not use insurance or copay info
- No formulary info
- Control for detailing and direct-to-consumer advertising
  - Robust to the addition of professional journal advertising and free samples

Benchmark models without learning

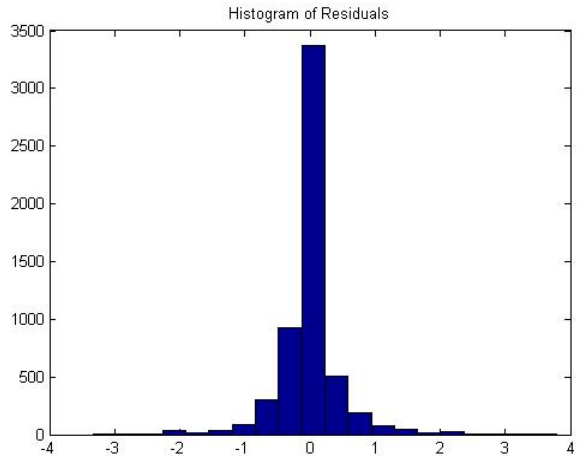
Dummy of Celebrex	-1.2584		-2.1166	
Dummy of Bextra	-10.7258	**	-1.0962	
(6-Satisf12345) for Celebrex	0.2933	***		
(6-Satisf12345) for Vioxx	0.2134	***		
(6-Satisf12345) for Bextra	1.7873	***		
Log Cum DTCA for Bextra	0.1949		0.5931	*
Patient female * Celebrex	0.2235	***	0.2126	***
Patient female * Bextra	-0.2242		-0.2729	**
Log L	-5008.7		-5071.9	
# of patients	2,062		2,062	
# of Rxs	5,688		5,688	

Summary from benchmark models

- With patient satisfaction and advertising
  - Patient satisfaction has an important impact on prescription choice, but all the advertising variables have no effect.
  - Impact of satisfaction greater for Bextra, probably because Bextra is newer than the other two drugs
  - On average, Celebrex is comparable to Vioxx but Bextra is significantly worse than both.
  - In terms of demographics, female patients are more likely to get Celebrex and less likely to get Bextra, as compared to Vioxx.
- Only advertising
  - Fit is worse than previous model
  - Results for Bextra advertising and for brand dummies counter intuitive

Estimation

- Step 1: We regress R_{pjt} on a full set of patient-drug (pj) dummies, and compute the residuals' standard deviation.
  - According to our model, this standard deviation gives us an unbiased estimate of σ_υ.
  - R-square 0.697, we get $\sigma_\upsilon = 0.496$



- Step 2: Use this value in estimating the remaining model parameters

Results from the learning model

	Risk Neutral		Risk Neutral Across-patient learning only		Risk Neutral within-patient learning only	
α_0	-8.1931	***	-471.0103	***	-4.4973	**
α_R	2.0675	***	112.2335	***	2.1473	***
σ_v	0.4960		0.4960		0.4960	
Q0_celebrex	-0.1974		0.3003		-0.2760	
Q0_bextra	-1.3771	*	1.2422		-2.1873	***
σ_{Q0} celebrex	0.0270	***	0.0002	***		
σ_{Q0} vioxx	0.0269	***	0.0002	***		
σ_{Q0} bextra	0.0398	***	0.0010	***		
σ_{q0}	0.3068	***			0.2682	***
Log Likelihood	-2738.1		-5036.5		-2816.7	
# of patients	2062		2062		2062	
# of Rxs	5688		5688		5688	

Results…. Continued

	Risk Neutral		Risk Neutral Across-patient learning only		Risk Neutral within-patient learning only	
Log cum DTCA	-0.3246	***	0.5632	***	-0.4522	***
Log cum Detailing	0.1340		-0.2806	*	0.5680	***
Patient Age * Celebrex	0.0079	***	0.0013		0.0076	***
Patient Age * Bextra	0.0000		-0.0049		0.0007	
Patient Female * Celebrex	0.1391	*	0.2253	***	0.1390	*
Patient Female * Bextra	-0.2714	*	-0.2678	**	-0.2804	*

Summary from learning models I

- Significant learning from patient satisfaction
  - α_R (+ and significant) implies doctors believe that satisfaction reports from patients are correlated with drug efficacy and use them to update the prior
  - Magnitudes of σ_{Qj0} are much smaller than both the noise in satisfaction report (σ_v) and the dispersion of patient-drug match (σ_{q0})
    - Doctors hold strong priors on average efficacy of the three drugs. Although they value satisfaction reports, updating on the general drug quality is slow.
    - Learning on the specific match between a drug and a patient is faster, because the magnitude of σq0 is much closer to that of συ.

Summary from learning models II

- No advertising variable has a significant, positive coefficient in the model that incorporates both types of learning
  - The coefficient for DTCA is negative and significant. Could indicate presence of factors correlated with advertising but we do not observe?
  - Ran benchmark models without satisfaction data for the period from 1999 to 2001 when Vioxx and Celebrex were launched in the market – strong positive effects of detailing and DTC
- Patient learning plays a much more important role in drug diffusion than does advertising. Doctors learn from patient satisfaction information but learning on the general drug quality, is gradual.
- Learning across patients and learning within patients are both important although latter seem more critical for our data

Summary from learning models III

- Prior estimates are largely as expected
  - Prior mean of Bextra is smaller than that of Vioxx and Celebrex, which is consistent with the relative market shares of the three drugs
  - Dispersion in the prior of Bextra is greater than that of the other two, which is consistent with the late entry of Bextra.

Main results

- Patient learning plays a much more important role in drug diffusion than does advertising.
- At the beginning of 2001 and upon the Bextra entry in January 2002, doctors held a strong prior belief about the relative efficacy of Celebrex, Vioxx and Bextra.
- Patient satisfaction signal is much noisier than the prior. Hence, doctors learn from patient satisfaction information but the learning is gradual.
- In comparison, none of the advertising variables have significant and positive impact on prescription choice in the 2001 to 2003 time period.
- Learning across patients and within patients are *both* important
- Within-patient learning explains more data variations than across-patient learning

On-going work

- Incorporate news/articles in the framework
- Include traditional NSAIDS as the outside good
- Distinguish time-dependent learning from unobserved patient heterogeneity
- The role of risk aversion
- Test information pooling by geographic area
- More robustness checks on advertising and insurance status

Tentative conclusion

- Doctors learn both across-patient and within-patient, but within-patient seems more important for Cox-2 in our data period
- Doctors held a strong prior on the average drug quality as of Jan, 2001
- We suspect the strong prior is defined by FDA, and advertising. Although advertisings do not play much role after 2001, they are highly influential in the diffusion before 2001.